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10/574,054	06/07/2006	Youe-Kong Shue	8031-011-US	7988

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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,054	SHUE ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/1/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of cartilage degradation, synovitis and subchondral bone edema, does not reasonably provide enablement for the prevention of the said conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The state of the prior art
(C) The level of predictability in the art
(D) The amount of direction provided by the inventor
(E) The existence of working examples
(F) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claims 31-33 are drawn to a method of preventing cartilage degradation comprising administering in mammals who have less sever said cartilage degradation comprising a therapeutically effective amount of N-acetylglucosamine. The scope of the claims is seen to

include the administration of the said compounds to a healthy mammal, and subsequent exposure to conditions that would cause the said cartilage degradation, wherein the said compounds prevent said exposure from manifesting itself in said mammal so exposed. The claim also recites less severe, which means that cartilage degradation has already taken place to some extend.

The state of the prior art

Prior art (Henderson, US 5,587,363) teaches the use of glucosamine and N-acetyl glucosamine for the treatment of osteoarthritis in the context of cartilage repair. The art is silent regarding the use of the active agents for the prevention of cartilage degradation.

The level of predictability in the art

Based on the teaching of the prior art above there is not seen sufficient data to substantiate the prevention of cartilage degradation as instantly claimed. Based on the teaching of Henderson the prevention of cartilage degradation is highly unpredictable.

The amount of direction provided by the inventor

Even though the instant specification provides references to the treatment of osteoarthritis it is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the prevention of cartilage degradation using active agent as instantly claimed.

The existence of working examples

The working examples set forth in the instant specification are drawn to the effect of the active agents on synovium and cartilage that have degraded to some extent, which is seen as treatment of the condition after its onset. One of ordinary skill in the art will not extrapolate the

results of the instant examples to the prevention of the said condition using the active agent as instantly claimed.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the prevention of cartilage degradation as instantly claimed. One of ordinary skill in the art would have to perform undue experimentation with the active agent to determine if the said active agent prevents the said joint condition

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6 and 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is

(a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 6 recites the broad recitation device, and the claim also recites pump which is the narrower statement of the range/limitation.

The term "less" in claim 31 is a relative term which renders the claim indefinite. The term "less" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 18-19, 22-24 and 27-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Henderson (US 5,587,363).

Henderson teaches the use of compositions comprising glucosamine for the treatment of connective tissue and cartilage repair and arthritis/pain. The aminosugar can be glucosamine or N-acetyl glucosamine or galactosamine or their salts (col. 3, line 34 through col. 4, lines 16-63;

col. 6, lines 49-56; col. 8, Case #1; col. 6, lines 48-56; col. 7, lines 57-61). According to Henderson, connective tissues of humans and animals are constantly subjected to stresses and strains that can result in afflictions such as arthritis, joint inflammation (sports related injury; col. 1, lines 23-31). Repair is done by manufacture of collagen, which needs proteoglycans and for the production of proteoglycans glucosamine is needed (col. 1, line54 through col. 2, line 51). Glucosamine is also known to localize in cartilage and joint tissues (col. 4, lines 47-52). Henderson also teaches dosages of the aminosugars for the said treatments (col. 8, lines 1-49; col. 11 line 15 through col. 12, line 46). This teaching of Henderson is seen to meet the limitations of the said instant claims.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Speck (US 4,870,061).

Speck teaches a method of treating degenerative joint disease (joint cartilage) by administration of N-acetyl glucosamine in combination with excipients via intraarticular, intramuscular, intravenous, or other injection or infusion methods (col. 1, lines 1-67; col. 5 line 15 through col. 6, line 34). This teaching is seen to meet instant claims 1-2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-30 are rejected under 35 U.S.C. 103(a) as being unpatentable Henderson (US 5,587,363) in view of Speck (US 4,870,061), Nanba et al (US 5,169,636), Burger (US 5,843,919), Woerly (US 5,863,551), Evans et al (US 6,506,785) and Wong et al (WO 00/68194).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The teachings of Henderson and Speck are as above. However, Henderson and Speck do not exemplify the use of aminosugars in the treatment of synovitis and subchondral bone edema and also the use of various forms of the composition comprising them like liposome, nanosphere suspension, implant gel, controlled release, etc and also the use of the aminosugars of their invention in combination with anti-inflammatory drugs and hexoaminidase inhibitors.

Nanba et al, drawn to liposomes, teach compositions comprising oligosaccharides comprising glucosamine and galactosamine residues entrapped by liposomes (col. 1, lines 60 col. 2, line 68). Phospholipids like distearoylphosphatidylcholine are suggested for use in the liposome preparations. Charged lipids like phosphatidylserine are suggested for use inorder to prevent leakage of the entrapped agents (col. 4, lines 8-27). The liposomes containing the aminosugars are made into particles having a diameter of about 0.03-0.8 microns (microspheres, col. 5, lines 43-46). According to Nanba liposomes are models for biological membranes and are effective in stabilizing drugs and achieving sustained release of drugs in vivo. The duration of the efficacy of drugs can be prolonged (col. 1, lines 25-28; lines 37-39). Even though Nanba teaches oligosaccharides comprising glucosamine and galactosamine residues, one of skill in the art will recognize that the monomeric aminosugars can also be use to make the same liposomal formulations.

Burger, drawn to arthritis/osteoarthritis, teaches the treatment of these conditions using compositions of comprising a combination glucosamine and N-acetyl glucosamine (col. 2, lines 19-44). The said compositions are preferably in the form of solutions, suspensions, gels, systemic implant or an injection or injection into an affected joint (col. 3, lines 20-56).

Woerly teaches polymer hydrogels as implants for treating tissue replacement and regeneration (col. 1, lines 5-18). Another aspect of his invention is the use of a polymer matrix (col. 5, lines 33-40 and lines 52-56). The polymer matrices can include aminosugars like glucosamine, N-acetyl glucosamine, galactosamine and N-acetylgalactosamine (col. 8, lines 31-34). Even though Woerly does not exemplify the use of such matrices for the treatment of specific conditions as instantly claimed one of skill in the art will recognize that such matrices

containing the monomeric aminosugars can be made and used for the treatment of degenerative diseases and conditions as instantly claimed.

Evans, drawn to cartilage degradation and subchondral bone, teaches a method of treating the same using antiinflammatory agents in combination with glucosamine in different forms and modes of administration for the treatment of articular cartilage degeneration including timed release and controlled release or a depot (abstract; col. 7, lines 49; col. 8, lines 3-31; col. 9, line 26 through col. 10, line 25). Even though Evans teaches the use of glucosamine and antiinflammatory agent sin combination with the compound of formula (I) of his invention, one of skill in the art will recognize that glucosamine and the antiinflammtory agents alone could be used in the said forms and modes of delivery for the said treatment since the use of glucosamine alone for the treatment of cartilage degradation is taught in the prior art. The Examiner would like to point out that even though Evans teaches method of prevention of the said conditions Example 1 (col. 36; lines 39-46) teaches that osteoarthritis was induced in animals before administration of the active agents. This is seen as a method of treatment and not prevention.

Wong et al teach that hexoaminidases catalyze the myriad of processes, one of which is cartilage erosion in arthritic subjects from over catabolism of glycosaminoglycans that fill the cartilage tissue. Wong specifically teaches development of iminocyclitols as inhibitors of hexoaminidases (page 1, line 5 through page 2, line 13; page 2, lines 33-39). This means that iminocyclitols can be used in combination with glucosamine and galactosamine and their salts and their N-acyl derivatives for the treatment of cartilage degradation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a formulation comprising amino sugars and use it in a method of treatment as

instantly claimed since the active agents and the methods of treatment using them individually are seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make compositions comprising aminosugars including various forms of compositions and modes of administration and use them in a method of treatment of cartilage degradation, synovitis and subchondral bone edema as instantly claimed since the use of active agents like glucosamine, galactosamine and iminocyclitols since aminosugars like glucosamine are responsible for the synthesis of proteoglycans needed for cartilage/tissue repair and the said aminosugars are well known agents for the said treatment as taught in the prior art above.

It is well within the purview of one of ordinary skill in the art to adjust ratios and substitute structurally similar active agents and make compositions in different forms since similarity in structure and function/utility entail motivation for use in the instant compositions and methods. One of skill in the art would also be motivated to look for other active agents and formulation that are more efficient and have enhanced beneficial effects.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See In re Kerkhoven, 205 USPQ 1069, CCPA 1980.

Conclusion

Claims 1-33 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang, Ph.D./
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